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FURAN DERIVATIVES OF GROUP III ELEMENTS

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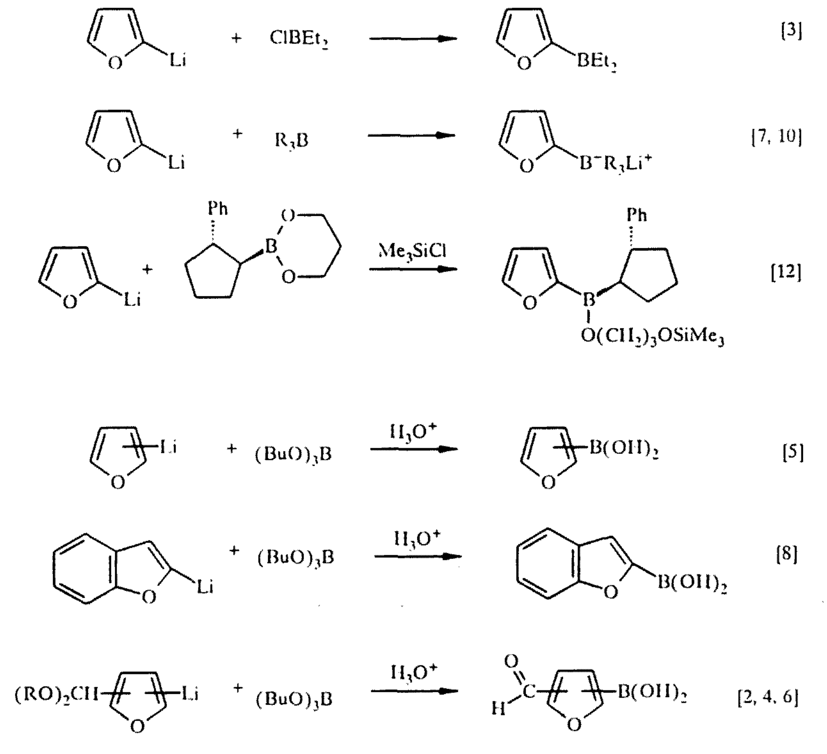
Methods for the synthesis of the furan derivatives of boron, aluminum, and thallium, the results from their physicochemical investigation, and their chemical transformations are summarized.

1. ORGANOBORON DERIVATIVES OF FURAN

1.1. Synthesis

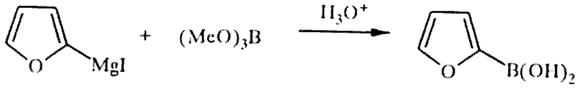
The lithium [1-12], magnesium [5, 13, 14], mercury [15], silyl [16], and stannyl [3] methods have been used for the synthesis of organoboron derivatives of furan in which the boron atom is directly attached to the heterocycle. Lithiofurans were used for the preparation of complexes with the boron derivatives R_3B or $RB(OR^1)_2$, and the products were subsequently used in the synthesis of alkylfurans [4, 10], alkenylfurans [11], optically active borinic esters [12], boronic acids of furan [5] and benzofuran [8], various boronic acids of formylfurans [2, 4, 6], and furyldialkylboranes [3].

All the possible isomers of the boronic acids of formylfurans were obtained by the reaction of 2- and 3-lithium-substituted dialkoxymethylfurans with tributyl borate followed by hydrolysis in an acidic medium [2, 4, 6].

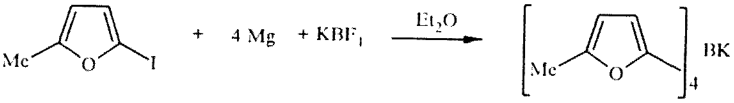


Latvian Institute of Organic Synthesis, Riga LV-1006. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 7, pp. 867-881, July, 1995. Original article submitted April 3, 1995.

Like the corresponding lithium derivative of furan, 2-furylmagnesium iodide can be used for the production of 2-furylboronic acid [14].

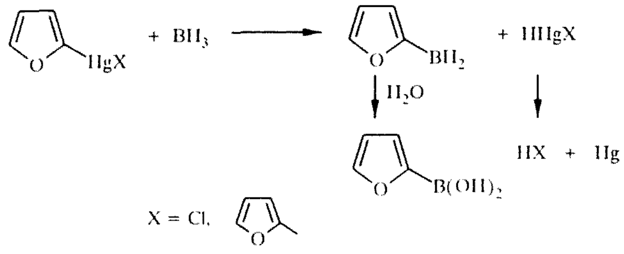


5-Iodosylvane reacts with magnesium and potassium fluoroborate with the formation of tetra(2-methyl-5-furyl)boriopotassium [17] (yield 7%).

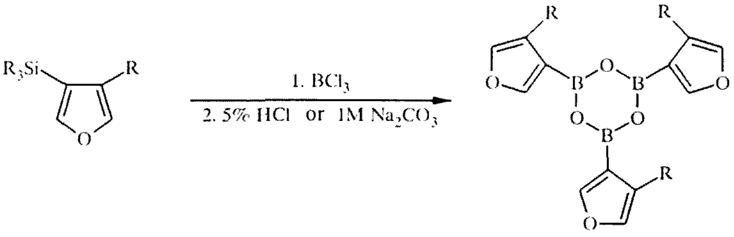


The analogous reaction with 2-iodofuran takes place with considerably greater difficulty (yield 2.5%), but it is nevertheless possible to obtain the tetra(2-furyl)borate in the form of the N-ethylpyridinium salt.

2-Furylboronic acid can be synthesized by the reaction of 2-furylmercury derivatives with a 10-fold excess of borane BH_3 in THF for 20 min at room temperature followed by hydrolysis with water [15]. In the opinion of the authors the reaction takes place through furylborane, which is formed as a result of transmetallation.

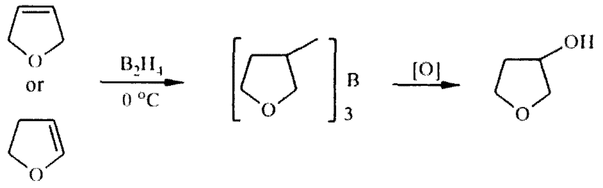


The silyl group in 3,4-bis(trimethylsilyl)furan and 3-aryl-4-trimethylsilylfurans undergoes regiospecific *ipso*-substitution under the influence of boron trichloride. Pyrolysis of the intermediate furyldichloroborates in an acidic or alkaline medium gave cyclotriboroxanes [16].



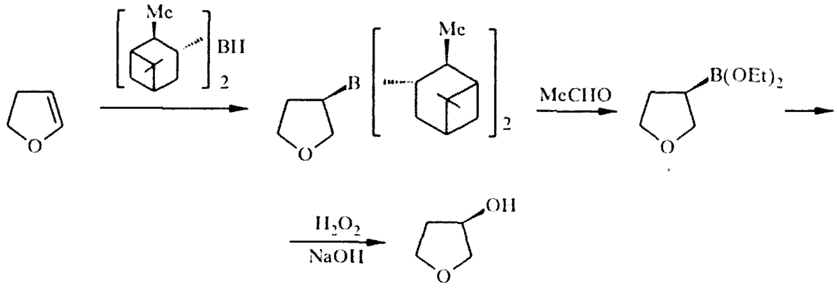
The reaction of trimethyl(2-furyl)stannane with diethylchloroborane Et_2BCl in benzene is exothermic. The product of this reaction is diethyl(2-furyl)borane [4].

Tetrahydrofuryl derivatives with a boron atom at position 3 of the heterocycle can be obtained easily by hydroboronation of dihydrofurans with boron hydride compounds [18, 19].

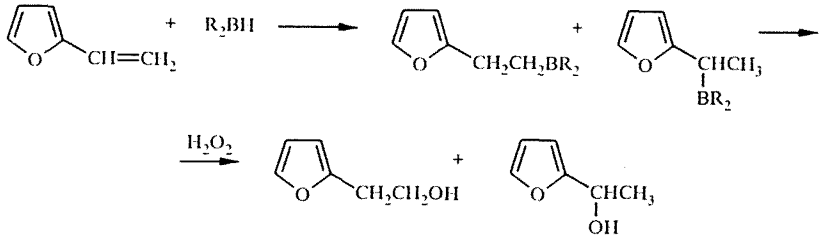


[18]

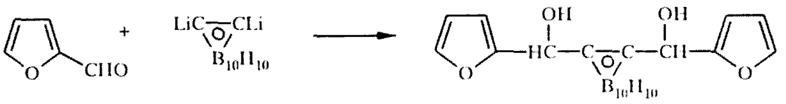
The asymmetric hydroboronation of 2,3- and 2,5-dihydrofurans was realized by means of di-(3-pinanyl)borane [19]. Thus, the hydroboronation of 2,3-dihydrofuran took place at −25°C. Subsequent substitution of the pinanyl group by an ethoxy group with acetaldehyde (a fourfold excess of the aldehyde, 6 h, 25°C) and oxidation with hydrogen peroxide led to 3-hydroxytetrahydrofuran having the R configuration at the asymmetric carbon atom. The analogous transformations of 2,5-dihydrofuran led to 3-hydroxytetrahydrofuran, but in this case the product was the S isomer [19].



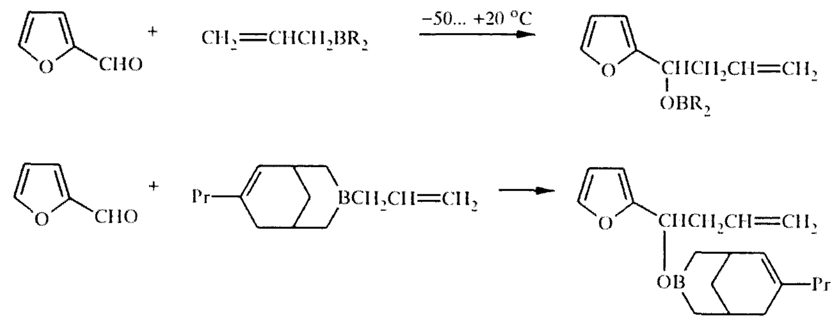
The most varied chemical transformations have been used for the synthesis of organoboron compounds of furan in which the ring and the boron atom are separated by a carbon and heterocarbon chain [20-32]. Thus, the hydroboronation of vinylfuran and 1-(2-furyl)-1-propene was realized with certain boron hydrides ($BH_3 \cdot Me_2S$, 9-borabicyclo[3.1.3]nonane, dicyclohexylborane) [20]. The main and, in the case of dicyclohexylborane, the only product is the β-product. Furfurylboran is formed in a small amount (3-6%) in the reaction with 9-borabicyclo[3.1.3]nonane and the complex of borane with dimethyl sulfide (Table 1).



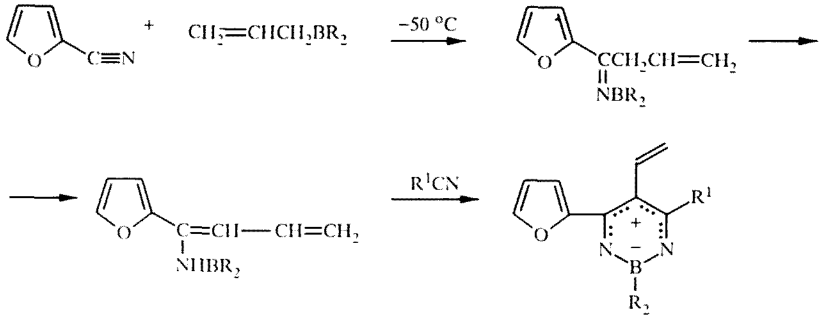
The lithium derivatives of dicarbadodecaborane [21] react with furfural according to the following scheme (yield 45%):



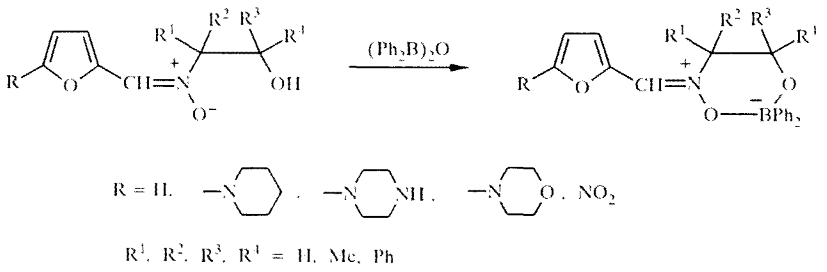
Furfural also enters into allylboronation with boranes $CH_2{=}CHCH_2BR_2$. The reaction takes place quickly with the release of heat and is not complicated by side processes [22].



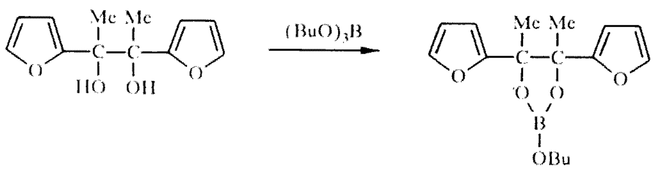
2-Furonitrile also enters into an analogous reaction [23]. However, the obtained iminoborane isomerizes under the influence of traces of water, alcohols, and amines to dienaminoborane, which undergoes cyclization with nitriles at +20°C.



Various furyl-containing nitrones also undergo cyclization in reaction with tetraphenyldiboroxane [24].

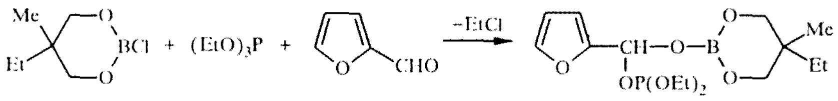


The reaction of 2,3-di(2-furyl)-2,3-butanediol with tributyl borate gives a cyclic borate [25]:

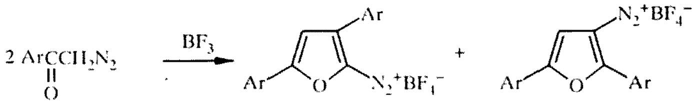


When heated with boric acid, tetrahydrofurfuryl alcohol gives a 22% yield of 2,3-dihydropyran and a certain amount of tri(tetrahydrofurfuryl) borate [26].

When furfural, triethyl phosphite $P(OEt)_3$, and 5-methyl-5-ethyl-1,3,2-dioxaborinane are heated gently, 2-[α-(diethoxyphosphinyl)furfuryloxy]-5-methyl-5-ethyl-1,3,2-dioxaborinane is formed with a 99% yield [27].



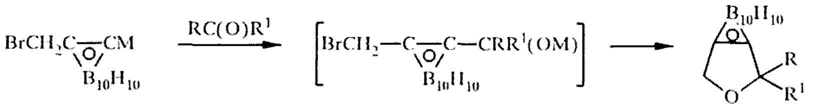
Furandiazonium fluoroborates were obtained from diaza ketones by the action of boron trifluoride [28, 29].



Compounds in which the furan ring and the boron atom are separated by an oxygen atom are formed during the action of dialkylboryl trifluoromethanesulfonate on butenolide in the presence of amines in dichloromethane at −78°C [30].

R = Bu, $c\text{-}C_5H_9$

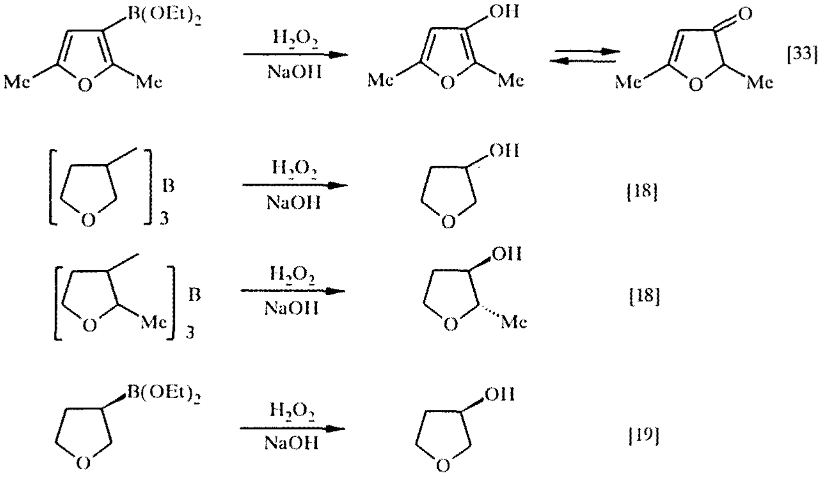
The tetrahydrofuryl derivatives of dicarbadodecaborane can be obtained during the cyclization of the lithium, sodium, and potassium derivatives of bromomethyldicarbadodecaborane with aldehydes and ketones [31, 32].



1.2. Properties

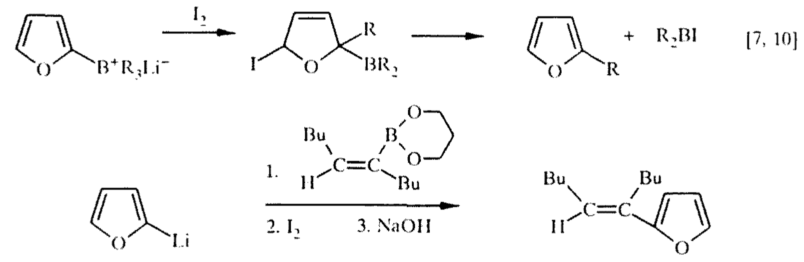
The reactions that organoboron compounds undergo can be divided into two groups. The first includes processes in which the furan–boron bond is cleaved, while the second include reactions taking place at the functional substituents at the boron atom.

The oxidation of furylboranes by hydrogen peroxide [18, 19, 33] takes place readily with the formation of the corresponding hydroxyl derivatives.

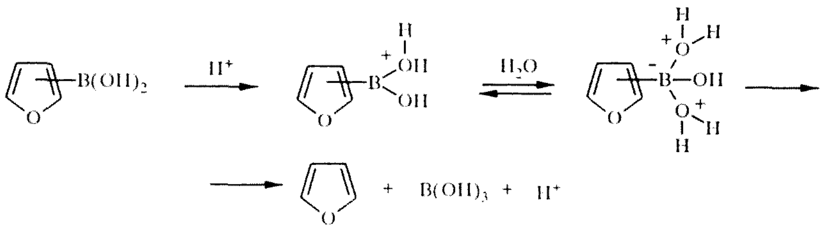


It should be noted that the oxidation of tri[3-(2-methyltetrahydrofuryl)]borane takes place selectively, and the *trans*-product is formed with an 80% yield [18]. The oxidation of (R)- and (S)-3-tetrahydrofuryldiethylboronates [19] takes place with retention of the configuration at the optically active carbon atom.

In the reaction of iodine and the complexes of furyllithium with trialkylboranes [7, 10, 11] (and this process can also be regarded as oxidation) various alkyl- and alkenylfurans were obtained with high yields.

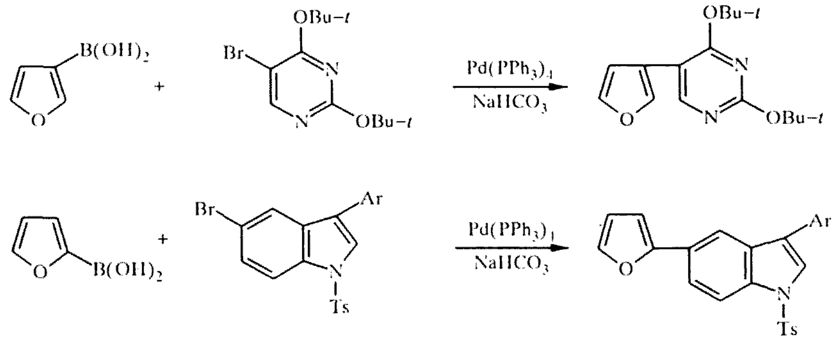


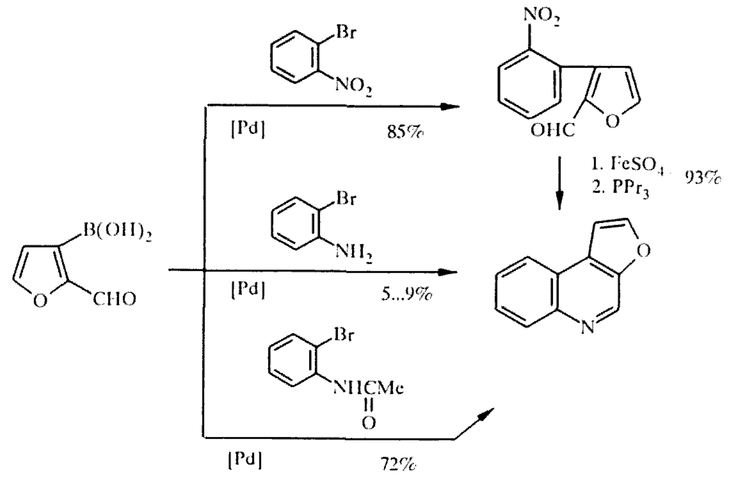
The 2- and 3-furylboronic acids [5, 34] and also their derivatives with formyl groups at various positions of the furan ring [34] are deboronated by the action of an aqueous solution of perchloric acid according to the following scheme:



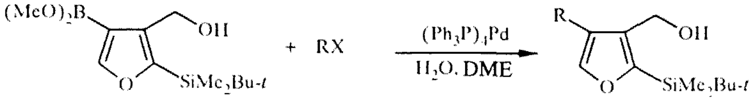
Boronic acids with the boron atom at the second position of the furan ring are deboronated more readily than the 3-isomers. The isotopic effect of this reaction ($k_{HClO_4}:k_{DClO_4}$) is greater than unity [34].

The cross-coupling of furanboronic acids with bromine derivatives and aryl triflates was used for the synthesis of biologically active compounds of the 5-substituted uracil [35], indole [36], furo[2,3-c]quinoline [37], and aryl- and alkenylfuran [9, 16] series. The reaction takes place in the presence of the palladium catalyst tetrakis(triphenylphosphine)palladium and sodium bicarbonate.





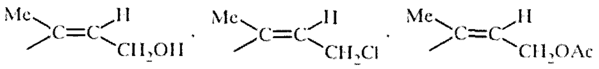
It was established in [9] that furyl borates, synthesized from the corresponding lithium derivatives, react with aryl bromides, aryl triflates, and alkenyl iodides in the presence of tetrakis(triphenylphosphine)palladium without isolation from the reaction mixture and form cross-coupling products in most cases with yields of 60-80%. Various 2,3,4-trisubstituted furans were obtained by this method from 2-dimethyl(tert-butyl)silyl-3-hydroxymethyl-4-furyl dimethyl borate, generated *in situ* [9].



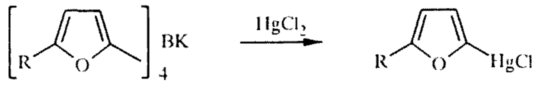
X = Br: R = Ph, α-$C_{10}H_7$, 4-MeC_6H_4, 2-$O_2NC_6H_4$, 2-$OHCC_6H_4$, $PhCH_2$

X = OTf: R = 4-$MeOC_6H_4$, 4-$O_2NC_6H_4$

X = I: R =

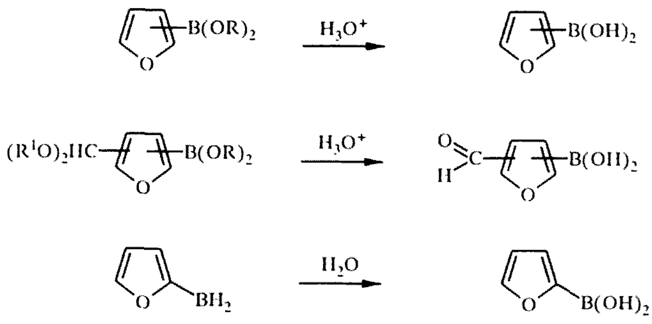


Tetrafurylboriopotassium compounds react with mercuric chloride at the $C_{(furyl)}-B$ bond. The products of this reaction are furylmercury chlorides [17].

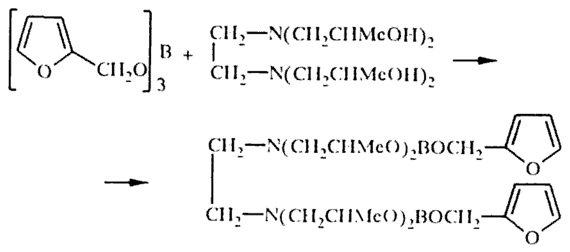


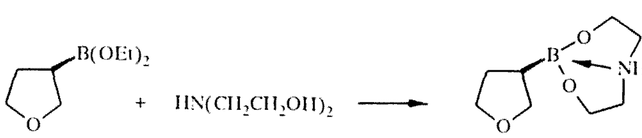
R = H, Me

Furylboronic [2, 5, 15], formylfurylboronic [2, 4, 6], and benzofurylboronic [8] acids were obtained by the hydrolysis of the corresponding diethyl- and dibutylboronic esters [2, 4-6, 8, 15] with a 1 M solution of hydrochloric acid at 0°C or of 2-furylborane [15] with water. Cleavage of the C–B bond is not observed under these conditions.



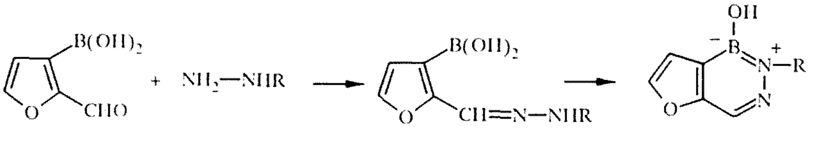
Furyl-containing borates [38] and boronates [19] enter into transesterification with ethanolamines.





In 3-tetrahydrofuryl diethylboronate one ethoxy group is substituted by the action of equimolar amounts of lithium acetylides $RC \equiv CLi$, and optically active borinates are formed [39].

3-(2-Formylfuran)boronic acid reacts slowly with hydrazine, methylhydrazine, and arylsulfonylhydrazines [4, 40-43]. The reaction does not stop at the first stage of condensation of the hydrazines with the carbonyl group (except in individual cases, e.g., with phenylhydrazine [4]), and intramolecular cyclization occurs with the formation of a diazaborine ring.



It was possible to obtain a cyclic product with phenylhydrazine during brief contact between the reaction mixture and dry hydrogen chloride in benzene and chloroform solution. Compounds of this type have bactericidal activity [42-44].

The pK_a values of 2- and 3-furylboronic acids and their formyl derivatives [5, 34] in water at 25°C were determined (Table 2).

2-Furylboronic ($pK_a = 7.89$) and 3-furylboronic ($pK_a = 8.65$) acids exhibit basic characteristics, and the introduction of the formyl groups significantly increases the acidity of the compounds. The only exception is 4-formyl-3-furylboronic acid ($pK_a = 7.96$), in which the aldehyde group has minimal effect.

Some furylboranes were studied by ^1H [2, 3], ^{11}B [3, 45], and ^{13}C [3] NMR spectroscopy. The results are given in Table 3.

With the introduction of a boron atom at the second position of the furan ring [diethyl(2-furyl)borane, tri(2-furyl)borane, (2-furyl)di(dimethylamino)borane, 2-furylboronic acid] descreening of the $H_{(3)}$ and $H_{(5)}$ protons is observed, and their signals are shifted downfield. This demonstrates the accepting effect of the boron atom on the π-electron system of the furan. The fact that the 2-furyl group exhibits donating character in the molecules of boranes follows from the ^{11}B NMR spectra. The boron atom in the molecule of tri(2-furyl)borane is strongly screened, while the screening in (2-furyl)-di(dimethylamino)borane is greater than in tri(dimethylamino)borane [3].

The distribution of π charge and the stabilization energy of 2- and 3-furylboranes were calculated by the *ab initio* method. The BH_2 group has a stabilizing effect on the furan ring, and this is more clearly defined for the 2-substituted furan [46].

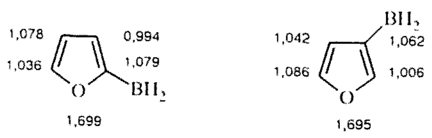
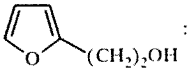
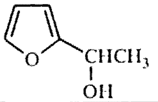
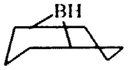
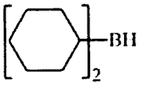
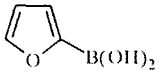
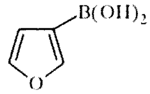
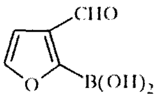
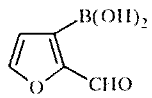
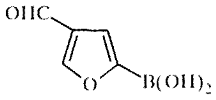
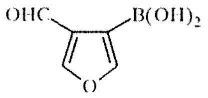
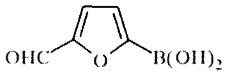
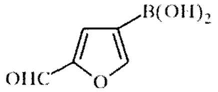


TABLE 1. Hydroboronation of 2-Vinylfuran (THF, 25°C)

Hydroborane	Ratio of products after oxidation with H_2O_2  : 
$BH_3 \cdot SMe_2$	87 : 13
	94 : 6 97 : 3 *
	100 : 0

*65°C.

TABLE 2. The pK_a Values of Furylboronic Acids

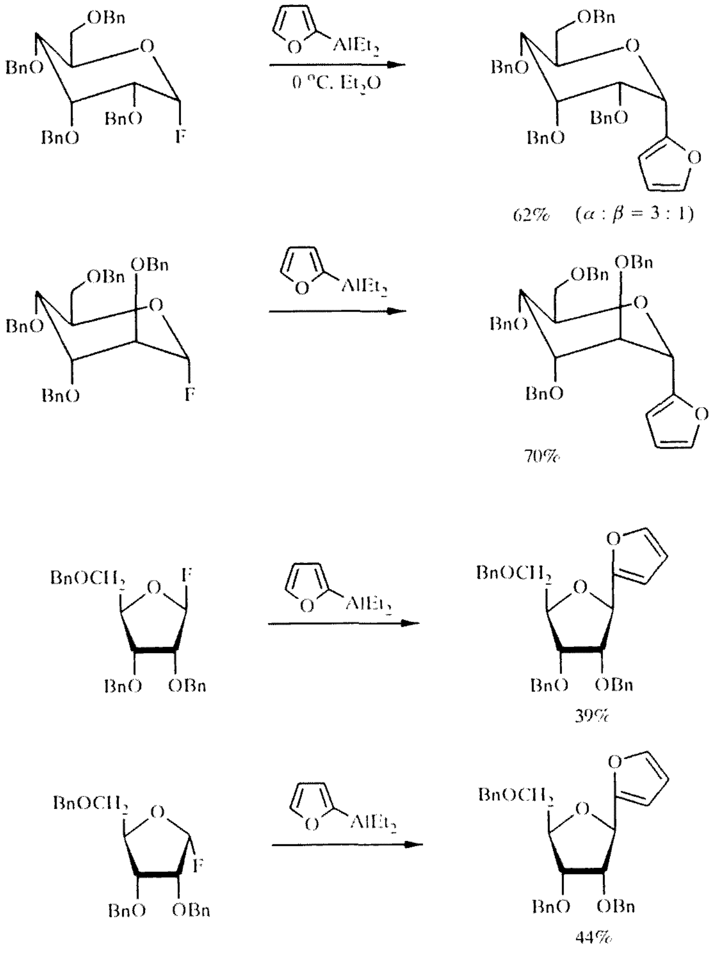
Compound	pK_a	Compound	pK_a
	7,89		8,65
	0,95		1,95
	2,15		7,96
	1,60		2,37

The structure of cyclotriboroxane with 4-trimethylsilyl-3-furyl substituents at the boron atoms was established by x-ray crystallographic analysis [16]. The molecule of this compound has C_{3h} symmetry with an average B–O bond length of 1.372 Å.

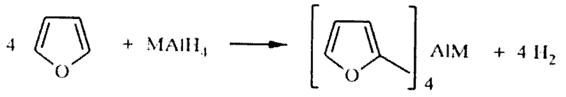
2. ORGANOALUMINUM AND ORGANOTHALLIUM DERIVATIVES OF FURAN

The synthesis and properties of the aluminum derivatives of furan have been studied little. Only two methods for the synthesis of aluminofurans with a $C_{furyl}-Al$ bond have been described in the literature [47, 48]. In one case the lithium method was used for the production of diethyl(2-furyl)aluminum [47].

The reaction of glycopyranosyl fluorides with diethyl(2-furyl)aluminum gave the corresponding furyl-containing sugars, and the reaction took place with retention of the configuration at the anomeric center. Coupling of the aluminum reagent with ribofuranosyl fluorides led to the β anomers. An anomeric mixture of ribofuranosylfurans (1:1) was obtained from the anomeric mixture of the initial fluorides by acid but not alkaline treatment [47].



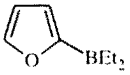
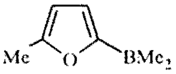
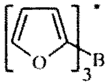
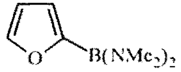
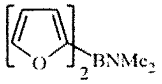
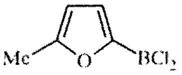
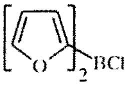
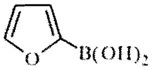
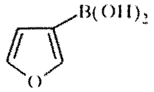
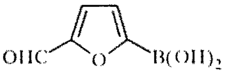
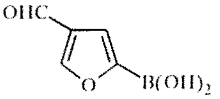
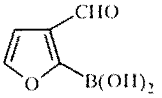
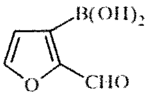
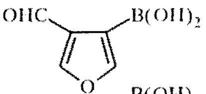
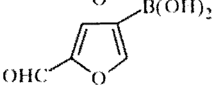
It was found that sodium and potassium aluminum hydrides metallate furan [48]. The reaction takes place in diglyme in 100-160°C. Subsequent treatment of the reaction mixture with carbon dioxide gave 2-furancarboxylic acid.



M = Na, K

In the analogous reaction with lithium aluminum hydride it was established that even prolonged heating only led to slight release of hydrogen.

TABLE 3. The ^{1}H and ^{11}B Chemical Shifts in the NMR Spectra of Furylboranes

Compound	$\delta^{11}B$, ppm	$\delta^{1}H$, ppm				Reference
		$H_{(2)}$	$H_{(3)}$	$H_{(4)}$	$H_{(5)}$	
	-67,6	—	7,30	6,50	7,75	[3]
	-66,2					[3]
 *	-35,0	—		6,56	7,78	[3, 45]
	-28,1	—	6,56	6,36	7,56	[3]
	-25,2					[3]
	-44,6	—	7,43	6,18	—	[3]
	-40,0					[3]
		—	7,03	6,39	7,69	[2]
		7,81	—	6,63	7,53	[2]
		—	7,27	7,50	—	[2]
		—	7,32	—	8,64	[2]
		—	—	6,87	8,00	[2]
		—	—	6,95	8,05	[2]
		8,07	—	—	8,77	[2]
		8,17	—	7,65	—	[2]

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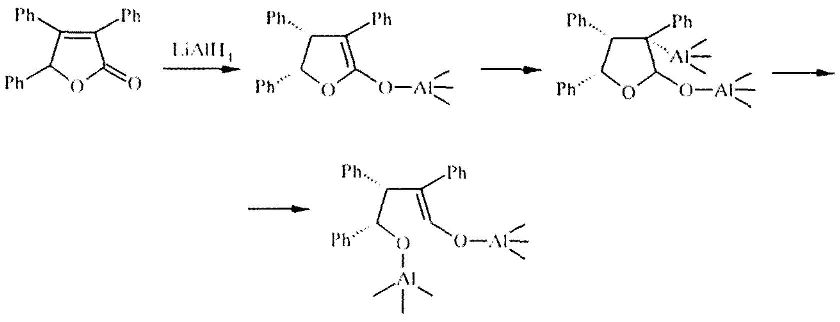
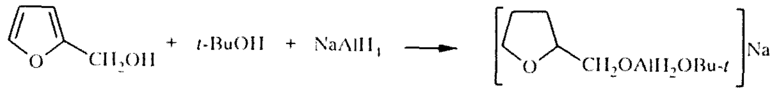
*^{13}C NMR spectrum (δ, ppm): $C_{(2)}$ — 160.7; $C_{(3)}$ — 160.6; $C_{(4)}$ — 111.5; $C_{(5)}$ — 148.7 [45].

A series of intermediate aluminum derivatives (including those with ring opening) are formed during the reduction of 3,4,5-triphenylfuran-2(5H)-one by lithium aluminum hydride [49]. Triethylaluminum opens the heterocycle of 2,2-diethylfuran-2(5H)one completely [50].

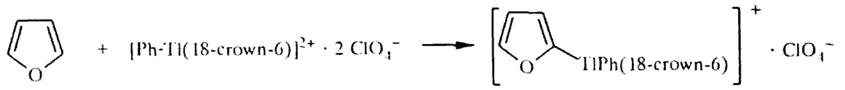
The conclusion about the structure of the aluminum derivatives was reached after analysis of the products from hydrolysis of these compounds by water and D_2O.



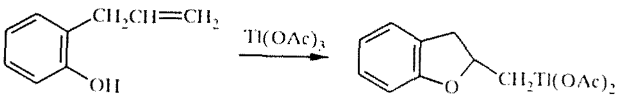
The reaction of sodium aluminum hydride, tert-butanol, and furfuryl alcohol gave a quantitative yield of sodium tert-butoxydihydro(tetrahydrofurfuryloxy)aluminate [51, 52], in which the aluminum atom and the heterocycle are separated by the OCH_2 group.



The first compound with a $C_{furyl}-Tl$ bond was obtained by electrophilic substitution of position 2 in the furan ring by the action of (18-crown-6)phenylthallium diperchlorate. The reaction took place under mild conditions at room temperature and gave a 67% yield [53].



A 2,3-dihydrobenzofuryl derivative of thallium is formed with a quantitative yield during the oxidation of o-allylphenol with thallium(III) acetate [54] in acetic acid at 0°C.



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